U.S. Pat nt Application 09/162,648

Cancer Immunotherapy using Allostimulated Cells in a Multiple Sequential Implantation Strategy

J.C. Hiserodt, Meyer Pharmaceuticals

Meyer Ref. SEQ-2

Claims

1. A method for treating cancer in a human patient, comprising:

   a) implanting at or around the site of a tumor in the patient a first cell population containing alloactivated lymphocytes that are allogeneic to leukocytes in the patient; and

   b) implanting at or around the site of a tumor in the patient a second cell population containing alloactivated lymphocytes that are allogeneic to leukocytes in the patient;

   wherein step a) and step b) are separated by an interval of at least three days, whereby the treatment stimulates a response in the patient against the tumor.

2. The method of claim 1, wherein the first cell population stimulates a response in the patient against the tumor before the implanting of the second cell population.

3. The method of claim 2, wherein the response comprises an inflammatory response.

4. The method of claim 2, wherein the response comprises an immunological response.

5. The method of claim 1, wherein the alloactivated lymphocytes in at least one of the cell populations are alloactivated against leukocytes of the human patient.,

6. The method of claim 1, wherein the alloactivated lymphocytes in at least one of the cell populations are alloactivated against leukocytes of a third-party donor different from the patient or the donor of the lymphocytes.

7. The method of claim 1, wherein the interval is between about one and eight weeks.

8. The method of claim 1, wherein the interval is between about two and twelve months.

9. The method of claim 1, wherein treatment according to the method has at least one of the following effects in at least 30% of treated subjects:

a) substantial regression of the tumor in size;

b) lack of recurrence of a tumor after removal; or

c) decrease in rate of formation of metastasis.

10. The method of claim 1, further comprising removing any residual tumor at or around the site of the second cell population at a time subsequent to when the second cell population was implanted.

11. The method of claim 1, wherein both the first and second cell populations have one or more of the following features:

i) contain between about 2×10^9 and 2×10^{10} cultured peripheral blood mononuclear cells originating from the donor and between about 1×10^8 and 2×10^9 cultured peripheral blood mononuclear cells originating from the patient or from a second donor;

ii) are obtained by a process in which donor lymphocytes are alloactivated by coculturing ex vivo with stimulator leukocytes for a period of about 48 to 72 hours; or

iii) are obtained by a process in which donor lymphocytes are alloactivated by coculturing ex vivo with stimulator leukocytes and harvested at about the time of initial alloactivation, measurable by acridine orange or CD69 assay.

12. A method for treating cancer in a human patient, comprising:

a) implanting at or around the site of a tumor in the patient a first cell population containing alloactivated lymphocytes that are allogeneic to leukocytes in the patient; and

b) implanting at or around the site of a tumor in the patient a second cell population containing alloactivated lymphocytes that are allogeneic to leukocytes in the patient;

wherein step a) and step b) are separated by an interval of at least three days, and wherein the cancer is selected from the group consisting of melanoma, pancreatic cancer, liver cancer, colon cancer, prostate cancer, and breast cancer.

13. A method for eliciting an anti-cancer immune response in a human patient, comprising:

a) implanting at or around the site of a tumor in the patient a first cell population containing alloactivated lymphocytes that are allogeneic to leukocytes in the patient; and

b) implanting at or around the site of a tumor in the patient a second cell population containing alloactivated lymphocytes that are allogeneic to leukocytes in the patient;

wherein step a) and step b) are separated by an interval of at least three days.

14. The method of claim 13, wherein the first cell population stimulates a response in the patient against the tumor before the implanting of the second cell population.

15. The method of claim 13, wherein treatment according to the method has at least one of the following effects:

a) substantial regression of the tumor in size;

b) lack of recurrence of a tumor after removal; or

c) decrease in rate of formation of metastasis.

16. The method of claim 13, further comprising removing any residual tumor at or around the site of the second cell population at a time subsequent to when the second cell population was implanted.

17. The method of claim 13, further comprising the step of removing any residual tumor at or around the site of the implanting of the second cell population at a time subsequent to step c).

18. The method of claim 13, wherein both the first and second cell populations have one or more of the following features:

i) contain between about 2×10^9 and 2×10^{10} cultured peripheral blood mononuclear cells originating from the donor and between about 1×10^8 and 2×10^9 cultured peripheral blood mononuclear cells originating from the patient or from a second donor;

ii) are obtained by a process in which donor lymphocytes are alloactivated by coculturing ex vivo with stimulator leukocytes for a period of about 48 to 72 hours; or

iii) are obtained by a process in which donor lymphocytes are alloactivated by coculturing ex vivo with stimulator leukocytes and harvested at about the time of initial alloactivation, measurable by acridine orange or CD69 assay.

19. A pharmaceutical composition comprising alloactivated lymphocytes allogeneic to leukocytes in a cancer patient packaged with information for the treatment of the patient according to the method of claim 1.

20. A pharmaceutical composition comprising alloactivated lymphocytes allogeneic to leukocytes in a cancer patient packaged with information for the treatment of the patient according to the method of claim 13.

21. *(New)* The method of claim 1, wherein tumor is not removed from the site at the time of implanting of the first cell population.

22. *(New)* The method of claim 23, wherein the second cell population is implanted into the same tumor site as the first cell population.